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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/471,749	12/23/1999	JENNIFER L. HILLMAN	PF-0519-1DIV	7908

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EXAMINER
HARRIS, ALANA M

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/471,749	HILLMAN ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,22,24,25,27-30 and 41-45* is/are pending in the application.

4a) Of the above claim(s) *24,25,29,30,41 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,22,27,28 and 43-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

1. The request filed on February 4, 2003 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/471749 is acceptable and a CPA has been established. An action on the CPA follows.

2. Claims 21, 22, 24, 25, 27-30 and 41-45 are pending.

Claim 21 has been amended.

Claims 24, 25, 29, 30, 41 and 42, drawn to non-elected inventions are withdrawn from examination.

Claims 21, 22, 27, 28 and 43-45 are examined on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 21, 27, 28 and 43-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 21 is broadly drawn to a biologically-active fragment, as well as a immunogenic fragment of SEQ. ID. NO:3 or SEQ. ID. NO:5 comprising at least 30 contiguous amino acid residues. Furthermore, the claim is drawn to naturally-occurring amino acid sequences having at least 90% sequence identity to SEQ IDNO: 3 or 5 having apoptotic activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the number of proteins broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Nor does the specification provide enablement for variants that have at least 90% sequence identity. Since the amino acid sequence of a protein determines its structural and functional properties, knowledge of which sequences of the amino acids would retain similar biological activity and immunogenicity the same as Applicants' is required. The specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful, especially in view of the non-conservative nature of the some of the changes that can be made according to the disclosure in the specification. And there is no guidance as to how to make sequences with 90% shared identity and capable of retaining apoptotic function. As set forth by Lazar et al. (Molecular and Cellular Biology 8(3): 1247-1252, March 1988) the data wherein substantiates the fact that the introduction of mutations in an amino acid sequence will yield products with different biological activity from the wild type protein. Notwithstanding, changes of 10% of a sequence will inevitably yield products that will not have the same structural characteristics or function as the native sequence.

The disclosure does not provide any information disclosing what fragments of SEQ ID NO:3 or SEQ ID NO:5 should be regarded as biologically active or immunogenic or what sequences in the native amino acid sequences can be mutated/changed to yield a 90% variant with apoptotic activity. The specification exemplifies no examples of the effective use of the sequences consisting of SEQ ID NO:3 or SEQ ID NO:5, nor fragments and variants of these polypeptides as a pharmacological agent, applicability to diagnostic assays or drug discovery. The scope of the claims must bear a reasonable correlation with the scope of enablement. In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to using the myriad of contiguous amino acid residues and variants encompassed in the scope of the claims, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

5. Claims 21, 22, 27, 28 and 43-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 21 broadly claims an isolated polypeptide comprising a naturally-occurring amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NOP 3 or SEQ IDNO: 5 having apoptotic activity. The written description in this instant case only sets forth SEQ ID NO:3 and SEQ ID NO: 5

consisting of 238 and 410 amino acids, respectively therefore the written description is not commensurate in scope with the claims drawn to naturally-occurring amino acid sequences sharing 90% sequence identity.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

With the exception of SEQ ID NO:3 and 5, the skilled artisan cannot envision the detailed structure of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written

description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". There is no disclosure, suggesting Applicants were in possession of sequence variants sharing 90% sequence identity with either SEQ ID NO: 3 or SEQ ID NO: 5. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

ALANA HARRIS
PATENT EXAMINER

Alana M. Harris, Ph.D.
June 15, 2003